Closing Keynote: Globalization and the Diplomacy of Science

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Editorial Note

The following is the text of the closing keynote address presented on the afternoon of Wednesday, December 9, 2009. Three responses followed.

Author's Note

The opinions presented in this text are those of the author and do not reflect the official policy or positions of the Botswana Harvard Partnership (BHP).

Abstract

The closing keynote address given by Dr. Joseph Makhema highlights the important issues that need to be understood in international research collaborations. Dr. Makhema uses his extensive experience in international research collaborations to illustrate the various challenges that collaborating partners in international research may face. He emphasizes that both diplomacy and justice are critical elements of international collaborative research.

Keynote

I thank the organizers for the invitation. The meeting comes at a unique time when there are efforts to strengthen capacity for both research-related activities and regulation of the research. Also, it comes at a time when there is unprecedented interest by various stakeholders in research linkages in Botswana. We at the Botswana Harvard Partnership certainly welcome all newcomers and hope that their efforts in Botswana and regionally shall drive research activities to a higher level, resulting in scientific research and new innovations actively contributing towards the diversification of the economy and development in Botswana. The conference also comes at the time when the School of Medicine is in its formative stages, so students, staff, and community members shall benefit from the outcome of deliberations. If the first two days of the conference are any indication, I can only hope that my presentation shall add value to the addresses that have preceded mine. I refer to the very pertinent key issues addressed in Archbishop Tutu's opening keynote address on *Human Illness and the Experience of Vulnerability,* and the various contributions of other speakers and presenters.

Advances in scientific research and development have largely been vested in the developed countries. There is no doubt that science drives economic growth and development. The phenomenal growth and discovery of new information technologies is

an indication of how that aspect has contributed to economic growth in some countries. Countries that have prioritized science, such as Japan, have leapfrogged over others in various indices of development.

The topic at hand is *Globalization and the Diplomacy of Science.*

My definition of globalization in science is as follows: It is the process of increasing the connectivity and interdependence of the world's scientific community in areas of research and scientific development. This definition has implications for the development of the physical and human infrastructure for scientific activities. It also implies homogeneity, benchmarking, uniformity of scientific processes, competencies and activities. Globalization in science, for me, is the trans-frontier ability to harness scientific and technological advances for the promotion of peace and sustainable development for the benefit of all countries individually and collectively!

Embedded in my utopian definition of the globalization of science is a moral and ethical obligation we have to ensure diplomacy, the equitable distribution of research and development opportunities, and of uniformity in scientific investment and resource allocation to ensure standardization of the physical and human infrastructure for scientific research and development. There are challenges to that definition, which is why I believe the organizers added the aspect of diplomacy… Hence, *Globalization and the Diplomacy of Science.*

Coming from an HIV/AIDS background, I have chosen to use the HIV/AIDS challenge as a case study to underpin various perspectives that relate to the topic at hand. Why? Because HIV/AIDS has catalyzed an unprecedented interest in global health. In turn, global health has been driven by the worldwide threat of new emerging diseases and different paradigms of the spread of diseases, such as severe acute respiratory syndrome (SARS), swine flu (HIN1), tuberculosis (TB) and malaria. HIV/AIDS and these emergent diseases have triggered new challenges for research and have stimulated collaborative approaches to address the problems they pose.

These disease-focused universal problems have encouraged decision makers in academic institutions—including those in the USA, Europe, and Japan—to prioritize and deploy resources for global health programs. These resources include investment in research, such as HIV research, to yield cost-effective and timely endpoints; this work needs to be located in high incidence geographic areas.

Vertical programs, such as the President's Emergency Plan for AIDS Relief (PEPFAR), contribute to infrastructural developments mainly for HIV/AIDS, but also increasingly offer concessions to holistic/integrated approaches to disease management, including operational research/strategic information. In addition, we are increasing multi-site and network trials, thus enhancing the training of research personnel.

This plethora of interest in global health is not without cost, as the targeted countries where research and programming is to be undertaken seek certain reciprocities, including: 1) upgrading and strengthening of local infrastructure and capacity development, such as skills transfer; 2) in-country institution and local IRB demands for in-country research, also

known as *the necessary ransom* (an example of some of the demands includes provision of study interventions beyond the research period); 3) improvement of science, technology, and local standards of care, and thus an increase in ethical obligations and challenges for research and study equipoise; 4) prioritization of resource allocation in regards to the conflict between care and research; 5) a research agenda based on local public health priorities and local participation in concept development and research design; and 6) local investigator involvement in the entire research process to be undertaken in the developing countries.

All the above posturing in the globalization process for research science and development demands a new form of diplomacy and understanding based on mutual respect and the recognition of each other's potential, role, and strengths. Clearly, research, development and science cannot, and should not, take place in an environment where the roles of the various stakeholders have not been clearly defined. There has to be a local principal investigator (PI), for example, when a multi-site network trial is to be undertaken. This person understands the relevant local cultural, environmental, and practical nuances that will impact the conduct of that research. The local PI would ensure that the application for the research meets local ethical and regulatory requirements prior to implementation. Research is not a franchise and should be contextualized to the local environment.

There are certain specific issues that are important to address in the context of Globalization and the Diplomacy of Science, once more using HIV/AIDS as a case study.

Resources

Most scientific resources for HIV/AIDS research and development have been and largely remain in the developed world. Until recently, investments in HIV/AIDS research were largely based on the scientific agenda for developed countries and research funding largely targeting developed world issues. Ninety percent of the budget for HIV/AIDS has been based on the B subtype of the virus, whereas 90% of the persons affected—70% of whom are in Sub-Saharan Africa—have contracted the C subtype. HIV vaccine design, investigational new drug (IND) research, and for that matter behavioural interventions, have been based on studies in the developed world.

While in certain areas such as drug efficacy, this approach has not had any negative impact, in some aspects such as HIV vaccines, there have been definite ramifications, including the failed Merck HIV vaccine trials. In this case, since the vaccine had adenovirus as the vector, there seemingly was an increased risk for HIV acquisition for the enrolled recipients who had high titres of adenovirus antibodies. This example demonstrates that research studies have to be undertaken in the environment where the intervention is to take place, including in the sub-population that shall be provided with the intervention. Very often these studies are undertaken as pilot projects, so they may not be instituted in an environment that is conducive enough to maximize testing of the concept and design. Notwithstanding benchmarking and standardization of research and scientific resources, researchers need to consider the applicability of the research design, irrespective of where the research and development (R&D) is to be undertaken.

Funding and Mechanisms of Funding

Funding has been obtained largely through competitive grant applications. This system has favoured investigators who have grant writing skills and proven research track records, and is a disincentive to upcoming scientists to apply for and receive money. Sources of funding have also been limited, with most being offered by the governments from developed countries and institutions such as the National Institutes of Health (NIH), the Bill and Melinda Gates Foundation, Wellcome Trust, and pharmaceutical companies. This situation has emanated from the high cost of conducting research, making it prohibitive for developing country governments and institutions to allocate money. For example, the cost of conducting an HIV Vaccine Trials Network Phase I study (HVTN protocol 048) in Botswana in 2003-2005 that enrolled 14 participants was $1million per year for the three years it took to complete this research. It would have been impossible for the BHP to secure such funding from the Ministry of Health Botswana. Globalization has, however, resulted in new funding opportunities offered by new sources such as PEPFAR, the Global Fund, and the European and Developing Countries Clinical Trials Partnerships (EDCTP) program. These funding sources have provided opportunities for new projects on HIV/AIDS in the developing countries.

Regulation and Legal Framework for Research and Development

As new resources and stakeholders have been attracted to developing countries for research and development, the regulatory framework for research has in some instances been found to be inadequate, and the capacities of the local ethics institutions have been overwhelmed by the volume of research and the complexities of the research process. IRBs have worked tirelessly to fulfill their mandate, very often with scarce resources. At this point, I wish to personally acknowledge and commend their dedication and commitment towards their work. The need to strengthen those institutions cannot be overemphasized. I believe, in a transparent and coordinated way, that there should be a globalized IRB-capacity strengthening process and mechanism, in much the same way as we undertake multi-site trials in an ethical manner that would not be deemed to be influencing the review process. The independence and autonomy of the IRB should also be protected and the scope of its work should be, in my opinion, of a scientific nature removed from political influences.

Community Issues

To avoid exploitation, it is essential to ensure a fair distribution of the benefits of research to the communities where such research is being undertaken. It is also important to avoid the displacing local medical staff from pressing community clinical care needs and to focus only on research, and to ensure that disruption to services where research is being undertaken is minimized. There is a fine balance between the need for healthcare providers to balance their participation in research with their role as healthcare providers. All research and development must ultimately take into account the ethical hazards that may be part of the social, economic, and political landscape of the community.

Specimen Banks, Sample Storage, and Shipping

Very often as part of research activities either to validate or confirm a finding, one needs storage of samples and specimens in the event that a particular endpoint necessitates testing primary samples. It may also be important to store specimens for future usage in the event that a new technique becomes available for retesting, or to group specimens due to rare occurrence of endpoints. Storage is expensive and requires reliable quality management (QM) systems, including stable sources of power and backup methods. Shipping samples to international labs is necessary for the standardization of multi-site trials, analysis using techniques that are not available locally, and for long-term storage under specific conditions that cannot be maintained locally. That said, genuine skills transfer and capacity building should in no way be sacrificed.

While this shipping may result in delays and conflicts with capacity building, it should be undertaken for the above reasons. The conditions for storage and shipping need to be clarified, with clearly defined policies and consent by protocols. Ultimately, there must be resourcing and the establishment of local specimen repositories.

Principal Investigators, Capacity Building, and Mentoring

This issue was discussed at this conference along with the challenges associated with the brain drain. It is essential to invest in and develop research infrastructure for the retention of scientists in developing nations and to foster ethos for research and development. It is also important to develop structures that protect research time for promising government or private employees, and to develop expectations that local researchers should lead and publish some aspects of their studies.

Access and Delivery of New Therapeutics

There are moral arguments for participants and communities of R&D to access products of research and INDs undertaken in their communities. This is based on their altruism and moral ethical obligation to do so.

Complexities of Care

HIV and most science projects are not easily simplified into vertical programs. There is a need for expansion of diagnostic and therapeutic capacity. Future trials are likely to bring about increasing laboratory complexity such as phenotypic testing and propriety issues, human leukocyte antigen (HLA) typing such as HLA*B5701, (a type of HIV that is slow to replicate), and co-receptor tropism such as Trofile, which measures the growth of HIV in response to different environments. There is an obvious need to reach out diplomatically to new partners in new fields.

Data Management

A study is only as good as the data it generates. Information technologies currently drive development, and concerted efforts to develop that infrastructure in the developing countries shall enhance and foster the *Globalization of Science.* Currently there are few bio-statisticians, programmers, and data analysts in developing nations.

Intellectual Property

There are cries to accept the intellectual property (IP) rights of scientists in developed countries and to develop systems and processes to protect those rights. This right to IP can come to fruition if local scientists are given the same opportunities to test their concepts and to lead and take part in network trials.

Recommendations

I would like to end by giving a few recommendations:

1. For globalization to occur, we need a Marshal Plan for Science to facilitate human and infrastructural development that elevates research and development infrastructure standards in developing nations to those practiced in developed countries—i.e., we must have institutions equivalent to the Massachusetts Institute for Technology (MIT) in Botswana—not only in Boston. We thus must have the financial resources to support local scientists, equipment, and reagents, and if not locally then regionally. In parallel, capacity building initiatives need to be strengthened to ensure demonstrable capacity to undertake the most complicated scientific research and development locally.

2. We need a harmonized approach to regulation in the same spirit as the International Conference on Harmonization. This could include the institution of a regional and international IRB for broader scientific perspectives and local IRBs for local cultural ethical reviews of concepts.

3. While endorsing network research like the Aids Clinical Trial Group (ACTG), the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT),and the HIV Vaccine Trials Network (HVTN), we should foster increased individually focused network capacitated research and training similar to the European & Developing Countries Clinical Trials Partnership (EDCTP), with a prescription for North-South, South-South collaboration.

Conclusion

In concluding, I wish to point out that, despite the aforementioned conflicts, I believe there has been demonstrable capacity for some local research and development, and that this capacity can be strengthened by the globalization of science. The current network multi-site model, although not perfect, is the basis for hope.

I will end now with a few words from Dr. Gerald T. Keusch, Director of the Fogarty International Center:

> *The future of science in developing countries requires investments in information technology, the creation of a culture of research ethics, and investments in modern science.*

I thank you, ladies and gentlemen.